

GGGGGGTGC GTGCTAGCTG (A/C) (G/A) GAGAC (G/A) GTGA (C $\gamma$ 1) [SEQ ID NO:23].

This primer panel has been previously used by the Assignee to amplify and clone the C2B8 anti-CD20 antibody (Nishioka et al., J. Immunol., 153:1027 (1994)) and numerous other mouse V<sub>k</sub> and V<sub>H</sub> gene segments (data not shown). - -

### **IN THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Non-elected claims 1 and 6-15 are canceled, claims 2-5 are amended, and new claims 16-39 are added.

1. (Canceled)

2. (Currently amended) An improved method of treating an autoimmune disease or disorder treatable by ~~modulating~~ inhibiting gp39 expression or ~~inhibiting~~ the gp39/CD40 interaction of gp39 with CD40, wherein said method comprises

obtaining and screening anti-gp39 antibodies to identify anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses; and

administering a therapeutically effective amount of ~~an antibody specific for gp39 anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses.~~

3. (Currently amended) The improved method of claim 2 wherein said disease or disorder is caused characterized by induction of IL- 2 secretion, and the anti-gp39 antibodies that are administered are substantially non-agonistic of IL-2 secretion by T cells.

4. (Canceled)

5. (Currently amended) The improved method of claim 4 2, wherein said autoimmune disease or disorder is selected from the group consisting of rheumatoid arthritis,

psoriasis, multiple sclerosis, diabetes, systemic lupus erythematosus and ITP idiopathic thrombocytopenic purpura.

6-15. (Canceled)

**New claims:**

16. (New) The improved method of claim 2, wherein said autoimmune disease or disorder is multiple sclerosis.

17. (New) The improved method of claim 2, wherein the anti-gp39 antibodies that are administered are chimeric or humanized antibodies having constant regions of human antibodies.

18. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered are chimeric "primatized"<sup>®</sup> antibodies having light and heavy chain variable regions of an antibody of an Old World monkey.

19. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered are humanized antibodies.

21. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered have heavy chain constant regions from a human antibody of isotype selected from gamma-1, gamma-3, and gamma-4.

22. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered comprise a light or heavy chain that has at least one conservative amino acid substitution.

23. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered comprise a heavy chain constant region having an amino acid substitution selected from the group consisting of

replacement of leucine with glutamic acid at Kabat position 236, and  
replacement of serine with proline at Kabat position 229.

24. (New) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered bind to the same epitope of gp39 as murine antibody 24-31.

25. (New) The improved method of claim 24, wherein the anti-gp39 antibodies comprise the complementarity determining regions of the 24-31 antibody light and heavy chain variable regions shown in Figure 7 (SEQ ID NO:27) and Figure 8 (SEQ ID NO:28), respectively.

26. (New) The improved method of claim 25, wherein the anti-gp39 antibodies comprise:

a humanized light chain variable region comprising an amino acid sequence selected from the group consisting of:

DIVMTQSPSFLSASVGDRVITTC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT  
GVPDRFSGSGSGTDFTLTISLQPEDFADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:1)

DIVMTQSPDSLAVSLGERATINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT  
GVPDRFSGSGSGTDFTLTISLQAEDVADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:2)

DIVMTQSPSFMSTSVGDRVITTC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT  
GVPDRFSGSGSGTDFTLTISMQPEDFADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:3) and

DIVMTQSPDSMATSLGERVTINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT  
GVPDRFSGSGSGTDFTLTISMQAEDVADYFC QQYNSYPYT FGGGTKLEIK;. (SEQ ID NO:4)

and a humanized heavy chain variable region comprising an amino acid sequence selected from the group consisting of:

EVQLQESGPGLVKPSETLSLTCTVSGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS  
RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTTLTVSS; (SEQ ID NO:5)

EVQLQESGPGLVKPSQTLSTCTVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS  
RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTTLTVSS; (SEQ ID NO:6)

EVQLQESGPGLVKPSQTLSTCAVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS

RISISRDTSNQFSLNLSVTRADTGVIYCAC RSYGRTPYYFDF WGQGTTLTVSS; (SEQ ID NO:7) and

EVQLQESGPGLVKPSSETLSLTCAVYGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS  
RISISRDTSKNQFYLLSSVTAADTGVIYCAC RSYGRTPYYFDF WGQGTTLTVSS. (SEQ ID NO:8)

27. (New) The improved method of claim 26, wherein the anti-gp39 antibodies that are administered have heavy chain constant regions from a human antibody of isotype selected from gamma-1, gamma-3, and gamma-4.

28. (New) The improved method of claim 26, wherein the anti-gp39 antibodies that are administered comprise a light or heavy chain that has at least one conservative amino acid substitution.

29. (New) The improved method of claim 26, wherein the anti-gp39 antibodies that are administered comprise a heavy chain constant region having an amino acid substitution selected from the group consisting of  
replacement of leucine with glutamic acid at Kabat position 236, and  
replacement of serine with proline at Kabat position 229.

30. (New) The improved method of claim 17, wherein the step of screening to identify anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses further comprises screening to identify anti-gp39 antibodies that do not compete for binding to gp39 with antibody murine antibody 24-31; and  
the anti-gp39 antibodies that are administered do not bind to the same epitope of gp39 as murine antibody 24-31.

31. (New) The improved method of claim 2, wherein the step of screening to identify anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses comprises assaying to determine the effect of an anti-gp39 antibody on the induction of production of at least one cytokine by T cells.

32. (New) The improved method of claim 31, wherein the step of screening to identify anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses comprises assaying to determine the effect of an anti-gp39 antibody on the induction of production of IFN- $\gamma$  or IL-2 by T cells.

33. (New) The improved method of claim 32, wherein the anti-gp39 antibodies that are administered inhibit the gp39-CD40 interaction and do not stimulate production by T cells of a cytokine selected from IFN- $\gamma$  and IL-2.

34. (New) The improved method of claim 2, wherein the step of screening to identify anti-gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of T-cell co-stimulation responses comprises assaying to determine the effect of an anti-gp39 antibody on T cell proliferation.

35. (New) The improved method of claim 34, wherein the anti-gp39 antibodies that are administered inhibit the gp39-CD40 interaction and do not stimulate T cell proliferation

36. (New) The improved method of claim 2, wherein the anti-gp39 antibodies are administered parenterally.

37. (New) The improved method of claim 17, wherein the anti-gp39 antibodies are administered parenterally.

38. (New) The improved method of claim 17, wherein the dosages of anti-gp39 antibodies that are administered are in the range of 0.05 to 100 mg per kilogram body weight per day.

39. (New) The improved method of claim 38, wherein the dosages of anti-gp39 antibodies that are administered are in the range of 0.5 to 10 mg per kilogram body weight per day.